Citation:

McMillan-Price J, Petocz P, Atkinson F, O'Neill K, Samman S, Steinbeck K, Caterson I, Brand-Miller J. Comparison of 4 diets of varying glycemic load on weight loss and cardiovascular risk reduction in overweight and obese young adults: a randomized controlled trial. *Arch Intern Med.* 2006 Jul 24;166(14):1466-75.

PubMed ID: 16864756

Study Design:

Randomized Controlled Trial

Class:

A - Click here for explanation of classification scheme.

Research Design and Implementation Rating:

POSITIVE: See Research Design and Implementation Criteria Checklist below.

Research Purpose:

To determine if diets of reduced glycemic load would increase the rate of fat loss, with minimal loss of lean mass, and improve cardiovascular disease risk factors.

Inclusion Criteria:

- 18 to 40 years of age
- Body mass index (BMI) ≥ 25
- Body weight < 150 kg
- Weight fluctuations < 5 kg in previous 2 months
- Willing to eat red meat
- Willing to maintain current physical activity

Exclusion Criteria:

- Chronic illness
- Regular medication other than birth control pills
- Eating disorders
- Special diets
- Pregnancy
- Food allergy
- Insufficient command of the English language
- < 18 or > 40 years of age
- BMI ≤ 25
- Body weight ≥ 150 kg
- Weight fluctuations ≥ 5 kg in previous 2 months
- Unwilling to eat red meat
- Unwilling to maintain current physical activity

Description of Study Protocol:

Recruitment

Recruited in Sidney, Australia using notice boards and newspaper advertisements.

Design: Randomized controlled parallel trial. Subjects were stratified according to weight (< 80 kg, 80-100 kg, > 100 kg) and sex and then randomly assigned to 1 of the 4 diets.

Blinding used: Not specified.

Interventions

4 reduced-energy, reduced-fat (30% energy), moderate fiber (30 g/d) diets

- Diet 1 = high-carbohydrate (55% energy) and average-protein (15% energy) based on high glycemic index whole grains, including fiber-rich breakfast cereals and breads
- Diet 2 = high-carbohydrate (55% energy) and average-protein (15% energy) based on previously verified low glycemic index foods
- Diet 3 = reduced-carbohydrate (45% energy) and higher-protein (25% energy) based on lean red meat and high glycemic index whole grains
- Diet 4 = reduced-carbohydrate (45% energy) and higher-protein (25% energy) based on previously verified low glycemic index foods

	Diet 1	Diet 1	Diet 2	Diet 2	Diet 3	Diet 3	Diet 4	Diet 4	
	Target	Actual	Target	Actual	Target	Actual	Target	Actual	*P value*
Carbohydrate, % energy	55	60 ± 1	55	56 ± 1	45	42 ± 1	45	40 ± 2	< 0.001
Protein, % energy	15	18 ± 1	15	19 ± 0	25	28 ± 1	25	26 ± 1	< 0.001
Fat, % energy	30	19 ± 1	30	22 ± 1	30	27 ± 1	30	29 ± 1	< 0.001
Alcohol, % energy	0	2 ± 1	0	3 ± 1	0	2 ± 1	0	3 ± 1	0.81
Glycemic index	67	70 ± 1	40	45 ± 1	57	59 ± 1	34	44 ± 1	< 0.001
Glycemic Load, g	127	129 ± 8	75	89 ± 5	87	75 ± 3	54	59 ± 4	< 0.001

Target glycemic load calculated as sum of foods in sample menus (glycemic index x carbohydrate content)

Statistical Analysis

- Primary end points were mean absolute change from baseline in body weight and fat mass at week 12.
- Pearson X^2 analysis was used to compare the proportion of subjects in each group who achieved 5% or more weight loss.
- Univariate and repeated-measures analyses of variance were used to assess the changes in weight, body composition, and blood parameters.
- Changes were assessed with and without adjustment for baseline differences.
- Missing data were replaced with the last known value for the primary intention-to-treat analysis and excluded in the secondary analysis.
- SPSS Version 12.0 was used for all statistical analysis.

Data Collection Summary:

Timing of Measurements

- Body composition was measured at baseline and on completion of the 12-week interventions.
- Weight was measured weekly.
- Blood parameters were measured at baseline, 6 weeks and 12 weeks.

Dependent Variables

- Body composition (dual-energy x-ray absorptiometry)
- Weight (electronic scales)
- Glucose
- Insulin
- Leptin
- Total cholesterol
- High density lipoprotein cholesterol
- Low density lipoprotein cholesterol
- Triglycerides
- Free fatty acids
- C-reactive protein
- Homeostasis model assessment (HOMA)

Independent Variables

4 reduced-energy, reduced-fat (30% energy), moderate fiber (30 g/d) diets

- Diet 1 = high-carbohydrate (55% energy) and average-protein (15% energy) based on high glycemic index whole grains, including fiber-rich breakfast cereals and breads
- Diet 2 = high-carbohydrate (55% energy) and average-protein (15% energy) based on previously verified low glycemic index foods
- Diet 3 = reduced-carbohydrate (45% energy) and higher-protein (25% energy) based on lean red meat and high glycemic index whole grains
- Diet 4 = reduced-carbohydrate (45% energy) and higher-protein (25% energy) based on previously verified low glycemic index foods

Control Variables

None indicated.

Description of Actual Data Sample:

Initial N: 129 enrolled (98 women, 31 men)

Attrition (final N): 116 (85 women, 31 men)

Age:

Diet 1	Diet 2	Diet 3	Diet 4
31.8 ± 1.7	30.5 ± 1.4	30.2 ± 1.5	34.6 ± 1.5

There were no significant differences in values listed above.

Ethnicity: Not provided.

Other relevant demographics:

	Diet 1	Diet 2	Diet 3	Diet 4
Number of Dropouts	5	2	1	5
Cholesterol, mmol/L	4.79 ± 0.19	4.71 ± 0.19	5.15 ± 0.18	4.83 ± 0.14
HDL cholesterol, mmol/L	1.29 ± 0.07	1.17 ± 0.05	1.16 ± 0.05	1.36 ± 0.08
HDL cholesterol ratio	3.94 ± 0.25	4.16 ± 0.24	4.75 ± 0.32	3.83 ± 0.26
LDL cholesterol, mmol/L	2.87 ± 0.16	2.90 ± 0.14	3.33 ± 0.15	2.89 ± 0.14
Triglycerides, mmol/L	1.37 ± 0.15	1.39 ± 0.13	1.41 ± 0.13	1.25 ± 0.12
Free fatty acids, υmol/L	510 ±33	436 ± 32	545 ± 42	520 ± 53
Glucose, mmol/L	5.04 ± 0.11	4.95 ± 0.07	4,92 ± 0.14	5.04 ± 0.09
Insulin, pmol/L	79 ± 7	83 ± 10	101 ± 12	81 ± 8
HOMA1-IR	2.6 ± 0.2	2.7 ± 0.4	3.1 ± 0.3	2.7 ± 0.3
HOMA2-IR	1.5 ± 0.1	1.5 ± 0.2	1.8 ± 0.2	1.6 ± 0.2
HOMA-%S	81 ± 8	85 ± 6	70 ± 6	82 ± 6
HOMA-%B	123 ± 6	122 ± 8	164 ± 24 (142 ± 10 without 1 outlier)	125 ± 8
Leptin, ng/mL	26 ± 2	22 ± 2	23 ± 2	22 ± 2
C-reactive protein, mg/L	3.6 ± 0.8	4.3 ± 0.7	3.1 ± 0.6	4.4 ± 0.9

There were no significant differences in any of the values listed above.

HDL = high density lipoprotein

LDL = low density lipoprotein

HOMA1 = original HOMA model

HOMA2 = updated HOMA nonlinear computer model

IR = insulin resistance

%S = insulin sensitivity

%B = β cell function

Anthropometrics

	Diet 1	Diet 2	Diet 3	Diet 4
Weight (kg)	86.0 ± 1.9	87.1 ± 2.7	87.7 ± 2.9	88.4 ± 3.0
Height (m)	1.68 ± 0.02	1.67 ± 0.02	1.66 ± 0.02	1.66 ± 0.02
Body Mass Index (BMI)	30.9 ± 0.6	30.6 ± 0.8	31.3 ± 0.8	32.1 ± 0.9
Waist (cm)	96.4 ± 2.0	96.8 ± 2.2	96.8 ± 2.2	98.2 ± 2.4

There were no significant differences in any of the values listed above.

Location: Sydney, Australia

Summary of Results:

Key Findings

- In the primary intention-to-treat analysis, all 4 diets resulted in weight reduction over 12 weeks.
- Reductions in weight, fat mass, and waist circumference were significant within each group ($P < 0.001$) but not among the 4 diets.
- There were significant differences in the proportion of individuals who lost 5% or more of initial body weight ($P = 0.01$)
  - Diet 1 = 31% of subjects
  - Diet 2 = 56% of subjects
  - Diet 3 = 66% of subjects
  - Diet 4 = 33 % of subjects
- The high-carbohydrate, low glycemic index diet (diet 2) produced the best clinical outcomes, reducing both fat mass and low density lipoprotein cholesterol (LDL-C).
- Participants who followed a high-carbohydrate, low glycemic index diet (diet 2) or a high-protein, high-glycemic index diet (diet 3) were twice as likely to achieve the clinical goal of a weight loss of 5% or more.
- Sex influenced fat mass changes, with a significant interaction with diet ($P = 0.008$)
  - Women who followed the high-carbohydrate, low glycemic index diet (diet 2) or the high-protein, high-glycemic index diet (diet 3) had an 80% greater fat loss compared with the conventional low-fat diet (diet 1; $P < 0.007$), without compromising lean mass.
- The high-protein, high glycemic index diet (diet 3) produced an increase in total and LDL-C concentrations (+8% overall, +10% in women) in contrast with the low glycemic index diets (P=0.01).
  - Overall, the glycemic index, but not the protein content, had a significant effect on change in total cholesterol levels ($P = 0.02$) and LDL cholesterol levels ($P = 0.009$).
- The conventional diet (diet 1) was associated with the highest level of postprandial glycemia as well as with the slowest rate of weight loss.
- The pattern of findings (changes in weight, waist circumference, fat mass, and lean mass) was unchanged in the secondary sensitivity analysis, from which subjects who had not completed the study were excluded (data not shown).
- Weight loss among the 4 diets was also similar when the analysis was confined to those with high fasting insulin levels (≥ 16 υIU/mL or 110 pmol/L, n = 37).
- Weight loss among the 4 diets was also similar when the analysis was confined to those with high fasting triglyceride levels (≥ 133 mg/dL or 1.5 mmol/L, n = 38).
- Subjects with high fasting triglyceride levels (≥ 133 mg/dL or 1.5 mmol/L) on the diet with the lowest glycemic load (Diet 4) achieved greater fat loss (-2.0 ± 0.8 [mean ± SE] kg, -4.9 ± 0.8 kg, -4.4 ± 0.9 kg and -5.6 ± 1.0 kg for Diets 1, 2, 3, and 4, respectively;$P = 0.03$).

Primary Intention-to-Treat Analysis of Changes in Weight and Body Composition

	Diet 1 (mean ± SE)	Diet 2 (mean ± SE)	Diet 3 (mean ± SE)	Diet 4 (mean ± SE)	Statistical Significance of Group Difference
All subjects (N = 129)	(n = 32)	(n = 32)	(n = 32)	(n = 33)	
Change in weight, kg	-3.7 ± 0.5	-4.8 ± 0.5	-5.3 ± 0.5	-4.4 ± 0.5	0.17
Weight change, %	-4.2 ± 0.6	-5.5 ± 0.5	-6.2 ± 0.4	-4.8 ± 0.7	0.09
Subjects with ≥ 5% weight loss, %	31	56	66	33	0.01
Change in waist, cm	-4.3 ± 0.7	-5.6 ± 0.7	-6.3 ± 0.6	-5,0 ± 0.7	0.22
Change in fat mass, kg	-2.8 ± 0.5	-4.5 ± 0.5	-4.3 ± 0.5	-3.7 ± 0.5	0.08
Change in lean mass, kg	-0.5 ± 0.2	-0.3 ± 0.2	-0.6 ± 0.2	-0.4 ± 0.2	0.75
Women (n = 98)	(n = 25)	(n = 23)	(n = 24)	(n = 26)	
Change in weight, kg	-3.1 ± 0.5*	-4.8 ± 0.5**	-5.4 ± 0.5***	-3.5 ± 0.5	0.006
Weight change, %	-3.7 ± 0.6	-5.7 ± 0.6	-6.5 ± 0.5	-4.1 ± 0.7	0.004
Subjects with ≥ 5% weight loss, %	25	61	75	23	< 0.001
Change in waist, cm	-3.2 ± 0.7	-5.8 ± 0.8	-6.2 ± 0.8	-3.9 ± 0.7	0.02
Change in fat mass, kg	-2.5 ± 0.5#	-4.5 ± 0.5##	-4.6 ± 0.5###	-2.9 ± 0.5#	0.007
Change in lean mass, kg	-0.2 ± 0.2	-0.3 ± 0.4	-0.2 ± 0.3	-0.1 ± 0.2	0.95
* Diet 1 vs. Diet 2, P = 0.009; Diet 1 vs Diet 3, P = 0.005 **Diet 2 vs Diet 4, P = 0.03 ***Diet 3 vs Diet 4, P = 0.02 #Diet 1 vs Diet 2, P = 0.01; Diet 1 vs Diet 3, P = 0.005 ##Diet 2 vs Diet 4, P = 0.04 ###Diet 3 vs Diet 4, P =					

0.02					

Primary Intention-to-Treat Analysis of Changes in Cardiovascular Risk Factors From Baseline to End of Week 12

Absolute Change	Diet 1 (n = 32)	Diet 2 (n = 32)	Diet 3 (n = 32)	Diet 4 (n = 33)	Statistical Significance of Group Difference
Cholesterol, mmol/L	0.05 ± 0.10	-0.18 ± 0.10*	0.24 ± 0.10*	-0.05 ± 0.10	0.04
HDL cholesterol, mmol/L	0.08 ± 0.04	0.03 ± 0.04	0.05 ± 0.04	0.07 ± 0.04	0.82
HDL cholesterol, ratio	-0.23 ± 0.11	-0.21 ± 0.11	0.02 ± 0.11	-0.37 ± 11	0.11
LDL cholesterol, mmol/L	0.04 ± 0.10	-0.17 ± 0.10**	0.26 ± 0.10**	-0.04 ± 0.09	0.02
Triglycerides, mmol/L	-0.14 ± 0.07	-0.05 ± 0.07	-0.18 ± 0.07	-0.19 ± 0.07	0.39
Free fatty acids, υmol/L	-63 ± 35	3 ± 36	-44 ± 35	-57 ± 34	0.56
Glucose, mmol/L	-0.04 ± 0.10	-0.06 ± 0.10	-0.05 ± 0.10	0.02 ± 0.10	0.94
Insulin, pmol/L	-8.1 ± 6.9	-13.3 ± 6.9	-17.1 ± 7.0	-10.4 ± 6.8	0.82
HOMA1-IR	-0.3 ± 0.2	-0.5 ± 0.2	-0.6 ± 0.2	-0.3 ± 0.2	0.72
HOMA2-IR	-0.1 ± 0.1	-0.2 ± 0.1	0.3 ± 0.1	-0.2 ± 0.1	0.77
HOMA2-%S	1.7 ± 7.3	9.3 ± 7.4	25.7 ± 7.4	16.4 ± 7.2	0.13
HOMA2-%B	-11.3 ± 17.8	-15.0 ± 17.8	-16.5 ± 18.1	11.8 ± 17.5	0.64
Leptin, ng/mL	-1.9 ± 1.5	-7.5 ± 1.5***	-5.4 ± 1.5	-1.0 ± 1.4***	0.006
C-reactive protein, mg/L	-0.8 ± 0.4	-1.1 ± 0.4	-0.8 ± 0.4	-0.01 ± 0.4	0.18

* Diet 2 vs Diet 3, $P = 0.03$

**Diet 2 vs Diet 3, $P = 0.01$

***Diet 2 vs Diet 4, $P = 0.01$

Other Findings

Nutrient Intake Determined From Food Diaries Completed at Baseline and During the Intervention

Variable	Diet 1	Diet 2	Diet 3	Diet 4	Statistical Significance of Group Difference
Energy, kJ					
Baseline	9630 ± 470	9030 ± 460	9220 ± 450	8890 ± 470	0.41
Interventions	6010 ± 240	6150 ± 190	5950 ± 170	5970 ± 190	0.90
Carbohydrate, g					
Baseline	262 ± 14	239 ± 13	248 ± 14	251 ± 19	0.78
Interventions	209 ± 9	200 ± 7	146 ± 6	143 ± 7	<0.001
Protein, g					
Baseline	99 ± 5	93 ± 5	89 ± 5	93 ± 4	0.54
Interventions	63 ± 3	69 ± 2	95 ± 2	93 ± 3	<0.001
Total fat, g					
Baseline	93 ± 6	82 ± 6	88 ± 5	73 ± 5	0.06
Interventions	32 ± 2	36 ± 2	44 ± 2	48 ± 2	<0.001
Saturated fat, g					
Baseline	36 ± 3	33 ± 3	32 ± 3	27 ± 3	0.16
Interventions	9 ± 1	10 ± 1	13 ± 1	13 ± 1	<0.001
Monounsaturated fat, g					
Baseline	33 ± 2	29 ± 2	31 ± 2	26 ± 2	0.10
Interventions	9 ± 1	11 ± 1	16 ± 2	17 ± 1	<0.001
Polyunsaturated fat, g					
Baseline	14 ± 1	13 ± 1	14 ± 2	10 ± 1	0.03
Interventions	4 ± 0	8 ± 0	6 ± 1	7 ± 0	<0.001
Fiber, g					
Baseline	23 ± 1	20 ± 1	19 ± 1	21 ± 1	0.14
Interventions	23 ± 1	30 ± 1	21 ± 1	24 ± 1	<0.001
Calcium, mg					
Baseline	984 ± 69	844 ± 79	824 ± 61	932 ± 62	0.30
Interventions	648 ± 47	637 ± 42	697 ± 44	719 ± 42	0.50
Iron, mg					
Baseline	13 ± 1	12 ± 1	12 ± 1	14 ± 1	0.21

Interventions	10 ± 1	11 ± 1	13 ± 1	13 ± 1	0.01
Zinc, mg					
Baseline	13 ± 2	11 ± 1	11 ± 1	12 ± 1	0.19
Interventions	8 ± 0	7 ± 0	11 ± 0	12 ± 1	<0.001

Author Conclusion:

- Both high-protein and low-GI regimens increase body fat loss, but cardiovascular risk reduction is optimized by a high-carbohydrate, low-GI diet.
- Dietary glycemic load, and not just overall energy intake, influences weight loss and postprandial glycemia.
- Dietary glycemic load may be more relevant to women than to men.
- Moderate reduction in glycemic load appear to increase the rate of body fat loss, particularly in women.
- Diets based on low glycemic index whole grain products (in lieu of whole grains with a high glycemic index) maximize cardiovascular risk reduction, particularly if protein intake is high.

Reviewer Comments:

This is a well-designed and conducted study. Authors note that diet goals for energy distribution were not met exactly.

Research Design and Implementation Criteria Checklist: Primary Research

Relevance Questions		
1.	Would implementing the studied intervention or procedure (if found successful) result in improved outcomes for the patients/clients/population group? (Not Applicable for some epidemiological studies)	Yes
2.	Did the authors study an outcome (dependent variable) or topic that the patients/clients/population group would care about?	Yes
3.	Is the focus of the intervention or procedure (independent variable) or topic of study a common issue of concern to nutrition or dietetics practice?	Yes
4.	Is the intervention or procedure feasible? (NA for some epidemiological studies)	Yes

Validity Questions		
1.	**Was the research question clearly stated?**	Yes
1.1.	Was (were) the specific intervention(s) or procedure(s) [independent variable(s)] identified?	Yes
1.2.	Was (were) the outcome(s) [dependent variable(s)] clearly indicated?	Yes
1.3.	Were the target population and setting specified?	Yes
2.	**Was the selection of study subjects/patients free from bias?**	Yes
2.1.	Were inclusion/exclusion criteria specified (e.g., risk, point in disease progression, diagnostic or prognosis criteria), and with sufficient detail and without omitting criteria critical to the study?	Yes
2.2.	Were criteria applied equally to all study groups?	Yes
2.3.	Were health, demographics, and other characteristics of subjects described?	Yes
2.4.	Were the subjects/patients a representative sample of the relevant population?	???
3.	**Were study groups comparable?**	Yes
3.1.	Was the method of assigning subjects/patients to groups described and unbiased? (Method of randomization identified if RCT)	Yes
3.2.	Were distribution of disease status, prognostic factors, and other factors (e.g., demographics) similar across study groups at baseline?	Yes
3.3.	Were concurrent controls used? (Concurrent preferred over historical controls.)	Yes
3.4.	If cohort study or cross-sectional study, were groups comparable on important confounding factors and/or were preexisting differences accounted for by using appropriate adjustments in statistical analysis?	N/A
3.5.	If case control or cross-sectional study, were potential confounding factors comparable for cases and controls? (If case series or trial with subjects serving as own control, this criterion is not applicable. Criterion may not be applicable in some cross-sectional studies.)	N/A
3.6.	If diagnostic test, was there an independent blind comparison with an appropriate reference standard (e.g., "gold standard")?	N/A
4.	**Was method of handling withdrawals described?**	Yes
4.1.	Were follow-up methods described and the same for all groups?	Yes
4.2.	Was the number, characteristics of withdrawals (i.e., dropouts, lost to follow up, attrition rate) and/or response rate (cross-sectional studies) described for each group? (Follow up goal for a strong study is 80%.)	Yes
4.3.	Were all enrolled subjects/patients (in the original sample) accounted for?	Yes
4.4.	Were reasons for withdrawals similar across groups?	Yes
4.5.	If diagnostic test, was decision to perform reference test not dependent on results of test under study?	N/A
5.	**Was blinding used to prevent introduction of bias?**	Yes
5.1.	In intervention study, were subjects, clinicians/practitioners, and investigators blinded to treatment group, as appropriate?	???

	5.2.	Were data collectors blinded for outcomes assessment? (If outcome is measured using an objective test, such as a lab value, this criterion is assumed to be met.)	Yes
	5.3.	In cohort study or cross-sectional study, were measurements of outcomes and risk factors blinded?	N/A
	5.4.	In case control study, was case definition explicit and case ascertainment not influenced by exposure status?	N/A
	5.5.	In diagnostic study, were test results blinded to patient history and other test results?	N/A
6.	**Were intervention/therapeutic regimens/exposure factor or procedure and any comparison(s) described in detail? Were interveningfactors described?**		Yes
	6.1.	In RCT or other intervention trial, were protocols described for all regimens studied?	Yes
	6.2.	In observational study, were interventions, study settings, and clinicians/provider described?	N/A
	6.3.	Was the intensity and duration of the intervention or exposure factor sufficient to produce a meaningful effect?	Yes
	6.4.	Was the amount of exposure and, if relevant, subject/patient compliance measured?	Yes
	6.5.	Were co-interventions (e.g., ancillary treatments, other therapies) described?	Yes
	6.6.	Were extra or unplanned treatments described?	Yes
	6.7.	Was the information for 6.4, 6.5, and 6.6 assessed the same way for all groups?	Yes
	6.8.	In diagnostic study, were details of test administration and replication sufficient?	N/A
7.	**Were outcomes clearly defined and the measurements valid and reliable?**		Yes
	7.1.	Were primary and secondary endpoints described and relevant to the question?	Yes
	7.2.	Were nutrition measures appropriate to question and outcomes of concern?	Yes
	7.3.	Was the period of follow-up long enough for important outcome(s) to occur?	Yes
	7.4.	Were the observations and measurements based on standard, valid, and reliable data collection instruments/tests/procedures?	Yes
	7.5.	Was the measurement of effect at an appropriate level of precision?	Yes
	7.6.	Were other factors accounted for (measured) that could affect outcomes?	Yes
	7.7.	Were the measurements conducted consistently across groups?	Yes
8.	**Was the statistical analysis appropriate for the study design and type of outcome indicators?**		Yes
	8.1.	Were statistical analyses adequately described and the results reported appropriately?	Yes
	8.2.	Were correct statistical tests used and assumptions of test not violated?	Yes
	8.3.	Were statistics reported with levels of significance and/or confidence intervals?	Yes
	8.4.	Was "intent to treat" analysis of outcomes done (and as appropriate, was there an analysis of outcomes for those maximally exposed or a dose-response analysis)?	Yes
	8.5.	Were adequate adjustments made for effects of confounding factors that might have affected the outcomes (e.g., multivariate analyses)?	Yes
	8.6.	Was clinical significance as well as statistical significance reported?	Yes
	8.7.	If negative findings, was a power calculation reported to address type 2 error?	N/A
9.	**Are conclusions supported by results with biases and limitations taken into consideration?**		Yes
	9.1.	Is there a discussion of findings?	Yes
	9.2.	Are biases and study limitations identified and discussed?	Yes
10.	**Is bias due to study's funding or sponsorship unlikely?**		Yes
	10.1.	Were sources of funding and investigators' affiliations described?	Yes
	10.2.	Was the study free from apparent conflict of interest?	Yes